I. REMARKS

The PTO requires the restriction of the claims in the above-identified application into one of the following nine groups of claims.

Group I: Claims 1-52, 59-61, and 79-85 allegedly drawn to an inositol 1,4,5-triphophate receptor (InsP3R) mutant.

Group II: Claims 53-58 and 62-67 allegedly drawn to a nucleic acid encoding a mutant inositol 1,4,5-triphophate receptor (InsP3R) mutant, a vector comprising a nucleic acid sequence encoding a mutant InsP3R, a cell comprising the vector comprising a nucleic acid sequence encoding a mutant InsP3R.

Group III: Claims 68-72 allegedly drawn to a method of screening for an agent that preferentially modulates calcium release phosphorylated InsP3R.

Group IV: Claim 73 allegedly drawn to a method of expressing a mutant InsP3R in a cell *in vivo*.

Group V: Claim 74 allegedly drawn to a method of treating a subject who has xerostomia, comprising introducing into the subject an expression vector comprising a nucleic acid sequence encoding a mutant InsP3R.

Group VI: Claim 75 allegedly drawn to a method of treating a subject who has cystic fibrosis, comprising introducing into the subject an expression vector comprising a nucleic acid sequence encoding a mutant InsP3R.

Group VII: Claims 86 and 87 allegedly drawn to a method of inhibiting apoptosis in a transplant in a subject comprising introducing a vector comprising a nucleic acid sequence encoding a mutant InsP3R.

Group VIII: Claim 88 allegedly drawn to a method of treating a subject with HIV, comprising introducing a vector comprising a nucleic acid sequence encoding a mutant InsP3R.

Group IX: Claim 89 allegedly drawn to a method of treating a subject with arthritis comprising introducing a vector comprising a nucleic acid sequence encoding a mutant InsP3R.

Applicants provisionally elect Group I with traverse.

The Examiner has also required further restriction if Group I is elected. The Examiner alleges that each of the mutants of Group I constitutes a distinct mutant comprising "a different

structure and biological activity." Accordingly, the Examiner requires the election of one of the mutants of claims 1-52, 59-61, and 76-85. Applicants provisionally elect the mutant of claim 28.

37 C.F.R. § 1.475 provides that national stage applications shall relate to one invention or to a group of inventions so linked as to form a single general inventive concept. Such inventions possess unity of invention. The requirement of a single inventive concept is fulfilled when there is a technical relationship within the claimed subject matter involving one or more of the same or corresponding special technical features. The special technical feature must define a contribution that the claimed subject matter makes over the prior art. Here, the Examiner characterizes the special technical feature as an InsP3R mutant; however, this alone can not be the special technical feature for it would not provide any contribution over the art. As noted in 37 C.F.R. § 1.475(a) the special technical feature are those features which define a contribution made over the prior art. Here the contribution is an InsP3R mutant comprising a substituted serine at the phosphorylation site. This technical feature is present in every claim and is not present in the prior art. Accordingly, the Examiner should reconsider the lack of unity with this technical feature in mind.

Applicants respectfully remind the Examiner that PCT Rule 13.2 states that

> the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

Additionally, MPEP 1850 states that contributions over the prior art "should be considered with respect to novelty and inventive step." Applicants respectfully point out that Mikoshiba (1997) Opinions in Neurobiology 7:339-345 does not destroy the novelty or inventive step of the common technical feature of this is application and thus does not anticipate or make obvious the inventive concept. In particular, and as noted above, the common technical feature of this application is an InsP3R mutant comprising a substitution of a serine at the phosphorylation site. This technical feature is present in every claim. The cited art does not teach serine substitutions (on page 339, the art specifically teaches Arg265, Lys508, Arg511, and Arg568). Moreover, the art does not teach let alone describe mutants at a phosphorylation site much less mutants at the phosphorylation site that comprise substituted serines. Because

Mikoshiba fails to teach all the limitations of the common technical feature, the reference does not anticipate the claims. Applicants additionally assert that no reading of Mikoshiba alone or in combination with the knowledge in the art renders the common technical feature obvious. Applicants have show that Mikoshiba does not disclose all the limitations of the common technical feature. Furthermore, there is no teaching anywhere in the Mikoshida that indicates where the phophorylation sites are located or provides any guidance that making a substitution at a phosphorylation site may be advantageous. Moreover, the Examiner has provided no teaching or disclosure that provides the elements missing from Mikoshiba. Therefore, the claims are not obvious either. Thus, the Examiner has not met his burden for establishing a lack of unity of invention. It is only the Examiners over simplification of the common technical feature that provides any support for a lack of unity rejection; however, as noted above, this is not an appropriate or legally sound reading of the common technical feature. Accordingly, Applicants submit that all of the pending claims possess unity of invention.

Moreover, Applicants respectfully point out that between Groups I - IX provide only 2 independent claims both of which the Examiner has indicated belong to Group I. The entirety of claims of Group II –IX depend from Group I. PCT Rule 13.4 states that:

> it shall be permitted to include in the same international application a reasonable number of dependent claims, claiming specific forms of the invention claimed in an independent claim, even where the features of any dependent claim could be considered as constituting in themselves an invention.

In fact, according to MPEP 1850, "unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. [emphasis added]" Moreover, it is stated in MPEP 1850 that "[i]f the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention." Therefore, because there are only two independent claims which includes a special technical feature which defines a contribution over the prior art which are both provided for in Group I, and because all of the remaining claims possess this technical feature by virtue of there dependency on said independent claims, all the pending claims possess unity of invention. Thus, the present restriction requirement is improper

and must be withdrawn. Accordingly, applicants respectfully request rejoinder and examination of all of the claims and at least Groups II – IX to the elected Group I.

Regarding the further restriction of specific mutants, Applicants are unclear from the Office Action whether the Examiner intended this to be a true further restriction or a species election. In the event this is a true restriction, Applicants respectfully remind the Examiner that 37 C.F.R. § 1.141(a) provides that "two or more independent and distinct inventions may not be claimed in one national application, except that more than one species of an invention…may be specifically claimed." Here applicants have provided a generic claim independent claim 1 which provides the common features of the genus of mutants that Applicants claim. Each of the mutants listed within groups I-IX comprises a species that shares the common features of this genus. Moreover, 37 C.F.R. § 1.141(a) provides that a reasonable number of species are allowable. Accordingly, the restriction is more appropriately a species election.

For the above reasons, reconsideration or withdrawal of the restriction requirement is requested.

No payment is believed to be due; however, the Commissioner is hereby authorized to charge any additional fees that may be required or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,
NEEDLE & ROSENBERG, P.C.

J. Gibson Lanier, Ph.D.
Registration No. 57,519

NEEDLE & ROSENBERG, P.C.
Customer Number 36339
678-420-9300
678-420-9301 (fax)

CERTIFICATE OF EFS-WEB TRANSMISSION UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being transmitted by EFS-WEB on the date indicated below.

J. Gibson Lanier, Ph.D. — Date: 3/10/08